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Comparison of Renal Transplantation Outcomes in Patients After Peritoneal Dialysis and Hemodialysis – A Case Control Study and Literature Review

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1. Introduction

For patients with end-stage renal disease renal transplantation is the treatment of choice. However, there is still some controversy if mortality rate after renal transplantation is affected by the chosen dialysis modality.

It is widely accepted, that in terms of survival hemodialysis (HD) and peritoneal dialysis (PD) are comparable. Especially in PD-patients with preserved residual renal function, control of hypertension is achieved more easily, whereas patients with diabetes mellitus do better on HD. In general, quality of life for patients is assumed to be better with PD than with HD [1].

In a cost-modeling strategy, incorporating quality of life and social perspective aspects in Scandinavia, it was shown, that the cost per quality-adjusted life year for PD was lower compared to HD in all analyzed age groups, whereas mean survival and frequency of transplantation did not differ [2].

Despite technological advance, only 15 % of the world dialysis population is managed by PD. Therefore, a "integrated approach" suggests starting PD in alarge percentage of patients, especially when renal transplantation is expected in the next 2 or 3 years after initiation of dialysis [3].

A very interesting point became obvious when analyzing data obtained from the Dialysis Morbidity and Mortality Study Wave 2, a national random sample of more than 4000 new dialysis patients in the USA enrolled during 1996 and 1997 and followed up until 2001. There, it was shown, that transplantation rates were significantly higher for patients reporting the greatest contribution to modality selection. These results support the association of patient

autonomy with transplantation and survival, probably in favor for patients actively choosing PD as their dialysis modality [4]. Also, a small Japanese single center study in 42 patients analyzed the effect of dialysis modality on rate of kidney transplantation from living donors and transplant outcome. There were no differences between the two modalities prior to transplantation in the graft survival rate, incidence of acute rejection, and complications before and after transplantation. However, The transfer rate from PD to transplantation was significantly ($p = 0.0036$) higher (4.7%) than that of HD (1.9%). Probably reflecting better cooperation between with the patients, their family and the provision of relevant information by nephrologists during PD [5].

2. Mortality on PD and HD

Although in 2005 the European Best Practice Guidelines for Peritoneal Dialysis conclude, on the basis of the available data, that peritoneal dialysis is a good treatment prior to renal transplantation there are contradictory survival rates reported in the literature for patients either on HD or on PD [6].

In 1995, data from the US Renal Data Systems from more than 170,000 patients showed, that prevalent patients treated with PD had a 19% higher adjusted mortality risk ($p < 0.001$) than those treated with HD [7].

In a comparable analysis obtained from the Canadian Organ Replacement Register, using data from 11,970 ESRD patients who initiated treatment between 1990 and 1994 and were followed-up for a maximum of 5 years was the mortality rate ratio for CAPD/CCPD relative to hemodialysis, as estimated by Poisson regression, was 0.73. There, the increased mortality on hemodialysis compared with CAPD/CCPD was concentrated in the first 2 years of follow-up and was detectable in all subgroups defined by age and diabetes status [8].

In contrast, a study comparing two year mortality rates of patients on the waiting list for renal transplantation to a historical prospective cohort of more than 12000 PD and HD patients disclosed, that especially for patients with a body mass index (BMI) of ≥ 26 mortality was increased with PD as dialysis modality [9].

Nevertheless, in a cohort of more than 3000 non-diabetic patients starting dialysis there was no difference in survival for patients treated either with PD or HD [10].

Also, in the well-known, prospective Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD) adjusted mortality rates between HD and PD patients were similar for the first two years. Thereafter, an increase in mortality especially in patients ≥ 60 years was detected [11].

Comparable results were seen in a prospective multicenter cohort study in 1041 patients (767 HD, 274 PD). There, the risk of mortality was equal in both groups for the first year with an increase in the second year. In addition, 25% of PD but only 5% of the HD patients switched their type of dialysis modality [12].

3. Renal transplantation in PD-patients – first experience

The first experience about the use of peritoneal dialysis in patients waiting for renal transplantation were published in some very early reports describing the feasibility of PD for patients awaiting renal transplantation[13-15]. Also in a small series of 15 patients the experience with renal transplantation in PD-patients was reported. Despite the fact, that some of the PD patients had peritonitis at the time of transplantation, no differences in graft survival were shown [16].

Similar results were published in an early study with a group of 44 patients, showing comparable results for patients with PD compared to HD patients[17].

Also, a small study in 9 PD patients reported significantly greater and longer wound drainage in PD patients. However, the incidence of acute rejection episodes, delayed graft function, graft arterial thrombosis and graft function recovery was not different [18].

4. PD versus HD and survival after renal transplantation

In a retrospective analysis of 61 PD and 159 HD patients there were no differences in survival of patients or grafts between the two treatment groups. One year after transplantation the percentages of survivors who had received continuous ambulatory peritoneal dialysis and hemodialysis were 88% and 91% respectively, and overall graft survival was 66% and 72%, respectively [19]. Similar results were reported from 42 PD patients, either treated with CAPD for more than 26 weeks or less than 26 weeks in comparison with 55 HD patients, irrespectively if treated with azathioprine + prednisolone or cyclosporine + prednisolone [20]. A retrospective analysis of 389 patients transplanted between Juli,1974, and July 1985, also evaluated the effect of dialysis modality on transplantation and mortality rates. By correcting for the influence of different variables and using time-dependent treatment co-variables, the bias adjusted estimates of the relative risk of death did not differ significantly from one another [21]. A cohort analysis of 500 first renal transplant recipients (241 on CAPD, 259 on HD) showed identical graft and patient survival after five years. However in 37 PD patients post-transplant peritoneal dialysis was necessary, while 10 patients developed peritonitis [22].

In 54 patients with renal transplantation after PD compared to 48 patients after HD with an immunosuppressive regimen consisting of prednisolone, azathioprine and cyclosporine there no significant difference in patient mortality and survival or graft survival between the groups. The incidences of infections were also similar in the two groups [23].

5. PD and complications after renal transplantation

There is some concern with respect for the risk of infections, especially peritonitis caused by the peritoneal catheter in PD patients. In a retrospective single center analysis the experience

with 18 renal transplantations in 16 PD patients was reported. In two cases cultures of the peritoneal catheter removed a few days after successful transplantation were positive. Nevertheless, with adequate antibiotic treatment none of the patients ever developed clinical peritonitis [24].

A cohort analysis of 500 first renal transplant recipients (241 on CAPD, 259 on HD) showed identical graft and patient survival after five years. However, 10 PD patients developed peritonitis [21]. Also, in a series of 100 patients undergoing simultaneous pancreas-kidney (SPK) transplantation (25 PD patients, 75 HD patients) frequency of abdominal infections, one year pancreas-graft survival rates, acute rejection episodes, kidney graft survival rates, or length of hospital stay did not differ between the two groups [25].

The question of peritonitis in peritoneal dialysis patients after renal transplantation was also addressed by a retrospective, single center study of 232 PD patients. In total, 30 peritonitis episodes with predominantly *Staphylococcus aureus* (10/30) or gram-negative bacteria (12/30) were observed. Risk factors associated with post-transplant peritonitis were the total number of peritonitis episodes, previous peritonitis with *S. aureus* bacteria, male sex, technical surgical problems at the time of transplantation, more than two rejection episodes, permanent graft non-function, and urinary leakage [26].

Comparable results are reported in a two-center study on post-transplant PD-related complications in 137 PD patients. There, only in a minority of the patients (n=19) PD-catheters were removed on the time of transplantation. In the remaining 118 patients the peritonitis rate was 7% [27].

In the European Best Practice Guidelines for Peritoneal Dialysis it is recommended to remove the catheter early after transplantation, nevertheless the catheter could be left in situ for 3–4 months despite a functioning graft. The guidelines also state, that peritonitis and exit site infections in transplanted patients should be treated using the ISPD guidelines 6.

In the last years the problem of post-transplant diabetes mellitus (PTDM) has gained more attention. A single center study reports on the occurrence of PTDM in 72 renal transplant recipients. In univariate analysis, the factors associated with the elevated risk of PTDM appearance were treatment by PD, older recipient age, positive family history of diabetes, hypertensive nephropathy as end-stage renal disease cause, higher body mass index at transplantation, and the graft from an older donor [28].

PD may be associated with an increased risk for graft thrombosis. At least, a single center experience revealed that in 915 consecutive renal transplantations CAPD was associated with a growing frequency of renal allograft thrombosis (7.3% vs. 3.6 %, $p < 0.02$). No differences in transplant characteristics, including hemodynamics, hematological parameters, immunosuppressive therapy, graft anatomy and preservation, were observed between the cases with graft thrombosis and a matched control group of 88 patients [29].

After renal allograft failure, patients may chose PD as their primary treatment option again. For this situation, it was shown, that after a failed renal transplantation PD-patients are prone to greater risk of death compared to PD-patients never transplanted. In addition, time to first

peritonitis, subsequent episodes of peritonitis, catheter change, or transfer to hemodialysis occurred at a much faster rate in patients with a failed transplant [30].

For patients returning to PD after graft failure, there may be a survival advantage in maintaining them on long-term immunosuppressive therapy. At least, a decision analytic model comparing the use of immunosuppression after transplant failure and return to peritoneal dialysis with immunosuppressive withdrawal, lead the authors to conclude, that there may be a survival advantage in maintaining patients on long-term immunosuppression [31].

6. PD and the occurrence of delayed graft function after renal transplantation

It is well known, that delayed graft function (DGF) and acute renal failure (ARF) after renal transplantation negatively influence short- and long-term graft outcome, therefore it is of interest to know if peritoneal dialysis affects occurrence or severity of DGF after renal transplantation.

A study in 250 patients (70 PD, 180 HD) evaluated the influence of dialysis modality on transplant outcomes. Among HD patients, 16% displayed DGF, versus 12% of PD patients. Multivariate analysis showed that factors affecting DGF were mode of dialysis, serum concentrations of parathyroid hormone and C-Reactive-Protein, and hemoglobin levels. Also after 3 and 5 years follow-up, PD patients showed fewer graft failures than HD patients (14% vs. 20%; and 17% vs. 28%[32].

In an analysis of 92 PD patients and 587 HD patients there was higher immediate graft function, less delayed graft function and less patients with never functioning grafts in the PD group. The groups were comparable except for a higher prevalence of diabetes ($p < 0.05$) and a shorter time on dialysis ($p < 0.01$) in PD patients [33].

A retrospective study in 40 PD and 79 HD patients receiving their first renal transplant analyzed the occurrence and frequency of DGF and acute renal failure. Both, DGF and ARF were observed less in the PD group than in the HD group. In a multivariate model, the authors could show that PD as pre-transplantation modality favorably modified the relative risk of developing DGF and ARF after renal transplantation[34]. A single center analysis in more than 650 patients (92 PD, 587 HD) reports a higher rate of DGF in HD patients (39.5% vs. 22.5%) and a higher rate of never functioning grafts in HD patients compared to PD patients (14% vs. 9%). When potential risk factors for DGF were compared, no relevant differences could be found [33].

Also for PD patients on automated peritoneal dialysis (APD), a retrospective matched-pairs study with 67 APD-patients showed favorable effects for PD on initial graft function (patients with a creatinine clearance below 10 ml/min 6 days after surgery) after post-mortem renal transplantation [35].

A recent retrospective single center analysis in 38 PD and 268 HD patients describes a higher incidence of DGF and primary allograft failure for HD patients, but was no difference in acute rejection episodes, long-term survivals, or renal function [36].

A case control study the incidence of DGF, defined as necessity to perform dialysis after transplantation, was analyzed in 117 PD and HD patients with a follow-up of 6 months. When matching the patients for age, sex, HLA compatibility PD-patients developed less DGF (23.1%) than HD patients (50.4%). In addition the decline of creatinine levels after transplantation was faster in PD patients. However, PD patients developed more acute rejection episodes, than HD patients, but creatinine levels after 6 weeks and 6 months were not different between the groups [37].

Besides a bundle of published single center experiences with renal transplantation in PD patients we do have at least two registry studies reporting on the effect of pre-transplant dialysis modality on renal transplant results.

Data from the United Network of Organ Sharing on all cadaveric graft recipients who were dialysis-dependent at the time of transplantation were analyzed with respect to different outcomes in the immediate post-transplant period for HD or PD patients. In total more than 9000 patients were evaluated, showing that PD patients were on dialysis for a shorter period of time, were more likely to be white, had a better HLA match, and had a lower PRA. After adjusting for comorbidities, the odds of oliguria were 1.60 times higher in black HD patients compared with PD patients and 1.29 times higher in white HD patients. Also, the odds of requiring dialysis in the first week were 1.56 times higher in black HD patients versus PD patients and 1.40 times higher in white HD patients. The rate of acute rejection was similar during the first hospitalization. Therefore, the authors suggest that there may be an association between hemodialysis and delayed graft function assuming that differences in biocompatibility between the two modalities could potentially be responsible [38].

A large retrospective analysis compared transplantation rates in PD and HD and outcomes after transplantation in more than 22000 patients from the years 1995 to 1998 in a US cohort. PD patients were more likely to be transplanted and their death censored graft failure was higher. However, mortality and overall graft failure were not different. Interestingly, the risk for early graft failure was higher for PD patients despite DGF was less common [39].

7. Own experience with PD and renal transplantation

Because of the in part contradictory data published in the literature we analyzed our own population of renal transplant recipients with the means of a retrospective case control study. Therefore, we chose 50 consecutive peritoneal dialysis patients transplanted since 1999. For match-pair-analysis, and as control group we selected the next hemodialysis patient subsequently transplanted after each PD patient. Follow-up data were available with a maximum of ten years after transplantation.

Kruskal-Wallis Test and Chi-Square-Test were calculated, with assuming a $p < 0.05$ as significant, for statistical purposes.

The PD-group consisted out of 28 male and 22 female patients with a mean age of 48.7 +/- 11.5 years (HD: 31 m, 19 w, 49.8 +/-13, p=n.s.) quite reflecting the German dialysis population. With respect to time on renal replacement therapy, cytomegalo-virus-status, HLA-mismatch, proportion of living donors, age, sex and initial immunosuppression there were no differences between the groups.

Although, during follow up more less PD-patients (n=3) than HD-patients (n=8) died, this difference did not reach statistical significance. With respect to graft failure, transplant loss (n=18) occurred significantly more in HD patients (n=13) than in PD patients (n=5). Nevertheless, mean serum-creatinine after 1, 2 and 5 years was not significant different between the groups. Also, delayed graft function was reported in only 4 PD patients compared to 10 HD patients (p<0.05).

To summarize, in our retrospective match-pair analysis patients on PD before renal transplantation developed less delayed graft function and had less graft loss during follow-up than patients on HD before transplantation.

8. Conclusion

Peritoneal dialysis (PD) is an established method of renal replacement therapy. PD and hemodialysis (HD) seem to be equivalent for long-term survival of the patients. Nevertheless, there is a beneficial effect of PD on patient survival after initiation of dialysis therapy. Probably, better preservation of residual renal function in PD patients compared to HD patients may be responsible for this effect.

Renal transplantation is the best treatment option for patients with endstage renal disease. The potential risk of infectious complications in PD patients after renal transplantation is attributed to the remaining PD catheter. However, this risk seems to be low and without effect on graft survival. For patients on HD a higher percentage of delayed graft function after renal transplantation is constantly reported in the literature. Nevertheless, long time patient and graft survival are not different between both treatment modalities.

Our own long-time clinical experience is congruent with the published literature and proves that peritoneal dialysis is a valuable treatment option for patients with end stage renal disease waiting for renal transplantation.

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